

**REMARKS/ARGUMENTS**

The office action of July 24, 2003 has been carefully reviewed and these remarks are responsive thereto. Reconsideration and allowance of the instant application are respectfully requested.

Claims 1-8, 14-15 and 17-22 remain pending in this application. Claims 1 and 14 have been amended, and claims 17-22 have been added. Claims 9-13 and 16 have been withdrawn without prejudice. Support for these amendments can be found in the claims as originally filed and throughout the specification. No new matter has been added by these amendments.

**REJECTIONS UNDER 35 U.S.C. §102**

Claims 1, 2, 4-8, 14 and 15 stand rejected under 35 U.S.C. §102(b) as being anticipated by Grinstaff (U.S. Patent No. 5,505,932). Claims 1, 2, 4-8, 14 and 15 also stand rejected under 35 U.S.C. §102(b) as being anticipated by Unger (U.S. Patent No. 6,416,740). Claims 1, 7, 8, 14 and 15 stand rejected under 35 U.S.C. §102(b) as being anticipated by Widder (U.S. Patent No. 4,849,210). These rejections are respectfully traversed.

Briefly, the present invention is directed to imaging compositions for use with multiple imaging modalities. The imaging compositions preferably include particles of metal compounds, such as gadolinium, zinc, magnesium, manganese, calcium and the like, with the metal compound particles incorporated in a microsphere shell. The microsphere shells may comprise protein substances. Use of the imaging compositions of the present invention allows for examination of a patient by multiple imaging techniques using a single dose in an in vivo administration of the imaging composition. Independent claims 1 and 14 have been amended to more particularly point out and distinctly claim the invention. Claim 1 as amended further

clarifies that the imaging compositions include microsphere shells having particles encapsulated between the walls of the shell and that the imaging compositions are characterized as being effective in a single dose in an in vivo administration for obtaining images using more than one imaging modality. Claim 14 as amended also further clarifies that more than one image can be obtained using more than one imaging modality with only a single administration of the imaging composition to a patient. Rejected claims 2 and 4-8 depend from claim 1, and rejected claim 15 depends from claim 14. New claims 17-22 depend from claim 14.

Grinstaff does not disclose or suggest such multi-modality imaging compositions or use of such multi-modality imaging compositions in a single-dose administration. Instead, Grinstaff discloses various organofluorine-containing compounds entrapped in polymeric shells for use as contrast agents. Although Grinstaff discloses that contrast agents that include small ferromagnetic or superparamagnetic metal particles, Grinstaff discloses that such contrast agents are suitable only for one imaging modality, namely magnetic resonance imaging. Furthermore, Grinstaff teaches that the particles are dispersed in a fluorocarbon or similar medium and then entrapped inside a polymeric shell. See col. 8, lines 38-44. Thus, the particles are not encapsulated within the shell material itself. Grinstaff does not disclose or suggest imaging compositions that include microsphere shells, the walls of the shell encapsulating one or more particles selected from the group consisting of gadolinium, zinc, magnesium, manganese, and calcium, that can be delivered a single time to a patient to then obtain images using two or more imaging modalities. Thus, Grinstaff does not disclose or suggest every element of the claimed invention.

Unger does not disclose or suggest imaging compositions having microsphere shells in which particles are encapsulated within the inner and outer walls of the shells and which may be used in a single administration to obtain images from two or more imaging modalities. Although the Office Action states that Unger discloses that the metals include manganese and gadolinium at columns 35-37, Unger discloses use of these metals in the form of their salts, not in particulate form. (See col. 5, line 35 – col. 6, line 24). Unger, however, does not disclose particles of metal compounds, including gadolinium, zinc, magnesium, manganese, calcium, with the particles encapsulated between the walls of a microsphere shell. Instead, Unger discloses paramagnetic and superparamagnetic contrast agents, including ferro- and ferrimagnetic compounds and the metal oxides of iron, manganese, cobalt and nickel. The contrast agents are entrapped within the internal void of the vesicle, administered as a solution with the vesicles, incorporated with any additional stabilizing materials or coated onto the surface or membrane of the vesicle. (See col. 37, lines 8-13). Thus, Unger does not disclose, teach or suggest imaging compositions that include microsphere shells having particles encapsulated within the shell material itself. Moreover, although Unger discloses various imaging modalities, Unger does not disclose a particular imaging composition that is suitable for use with more than one imaging modality in a single administration to the patient. Thus, Unger does not teach every element of the claimed invention as required under 35 U.S.C. §102.

Widder does not disclose or suggest imaging compositions that include particles of metal compounds, including gadolinium, zinc, magnesium, manganese, calcium, encapsulated within the walls of a microsphere shell, where the imaging compositions can be used with two or more imaging modalities. In particular, Widder does not teach a microsphere shell. Rather, Widder

discloses solid microspheres of superparamagnetic contrast agents, e.g., ferromagnetic iron compounds, suspended in a matrix material. Furthermore, Widder only discloses that the contrast agents are suitable for use with a single imaging modality, magnetic resonance imaging. Thus, Widder does not teach every element of the claimed invention.

**REJECTIONS UNDER 35 U.S.C. §103**

Claims 1-8, 14 and 15 stand rejected under 35 U.S.C. §103 as being unpatentable over any one of Grinstaff, Unger or Widder in view of Gordon (U.S. Patent No. 4,735,796).

As discussed above, Grinstaff, Unger and Widder do not disclose, teach or suggest imaging compositions that include particles of metal compounds encapsulated between the walls of a microsphere shell, where use of the contrast agents allows for examination of a patient by multiple imaging techniques using a single dose of an imaging composition. Gordon does not provide any teachings to overcome the deficiencies of Grinstaff, Unger or Widder. Gordon discloses use of ferromagnetic, diamagnetic and paramagnetic particles in the treatment and diagnosis of disease. Gordon does not disclose that the particles are incorporated in a microsphere shell. Further, Gordon does not disclose that the particles can be administered in a single dose to obtain images using two or more imaging modalities. Thus, even if any one of Grinstaff, Unger or Widder were combined with Gordon, their combination would not result in the presently claimed invention.

Accordingly, none of the cited references, either alone or in combination, disclose, teach or suggest the invention claimed in claims 1-8 and 14-15 or new claims 17-22, and the claims are not obvious.

**CONCLUSION**

It is believed that no fee is required for this submission. If any fees are required or if an overpayment is made, the Commissioner is authorized to debit or credit our Deposit Account No. 19-0733, accordingly.

All rejections having been addressed, applicant respectfully submits that the instant application is in condition for allowance, and respectfully solicits prompt notification of the same.

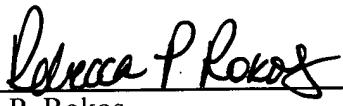
The Examiner is invited to contact the undersigned if necessary to facilitate prosecution of this application.

Respectfully submitted,

BANNER & WITCOFF, LTD.

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By:

  
Rebecca P. Rokos  
Registration No. 42,109

10 S. Wacker Drive, Suite 3000  
Chicago, Illinois 60606  
Tel: (312) 463-5000  
Fax: (312) 463-5001